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# THE CLINICAL ASPECTS OF "JUVENILE GENERAL PARALYSIS,"

WITH AN ACCOUNT OF A CASE TREATED WITH "606,"  
AND OBSERVATIONS ON PROPHYLAXIS.

*References to 1911.*

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THE history of juvenile general paralysis bears a curious resemblance to that of many other diseases once considered rare, now generally recognised as of comparatively frequent occurrence. Its existence was unknown until 1877, when Clouston published a description (1)\* of his first case in a boy, aged 16 years, under the name of "developmental general paralysis," and showed that it resembled, both clinically and pathologically, the form up to then considered exclusively confined to adult life. Two years later a second case was described by Turnbull in a child aged 12 years (2), and again two years later similar isolated examples by Nolan and Wiglesworth (3). It was in the same year that Regis recorded the first case on the continent (4). The condition was still considered very rare. Nevertheless, in 1895 Alzheimer had collected 40 cases, including 3 of his own (5), and in 1898 Thiry (6) had raised the number of known cases to 69. In 1900 Mott (7) published an elaborate analysis of 22 cases, collected in three years, from the London County Asylums alone, in 1908 he had raised the number of cases observed by him to 40 (8), and in 1910 to 60 (9). In the last 10 years cases have been recorded with increasing frequency from many other countries, till now there must be several hundreds in the literature, and it is not surprising to find that Fennell (10), as

\* The parenthetical figures occurring throughout the article refer to the bibliography at the end.

the result of his observations at Darenth, came to the conclusion that 5 per cent. of imbecile children were congenital general paralytics.

It will thus be seen that either the condition is becoming more frequent or else is being more readily diagnosed. Probably both suppositions are correct, yet undoubtedly, although the alienist is now constantly on the lookout for such cases, the medical profession as a whole has not yet grasped either their importance or their frequency: and, considering their invariably fatal termination, sufficient stress has not been laid on the paramount importance of treating every child, of known syphilitic parents, giving a positive Wassermann, whether it shows signs of congenital syphilis or not, as carefully as if it were an adult with definite symptoms of the disease: for it is a peculiarity of juvenile general paralysis that many of these children show absolutely none of the stigmata of congenital lues, though nearly all give a positive Wassermann.

It seems scarcely necessary now to labour the point of the close connexion between general paralysis and syphilis. Gowers and Ferrier always maintained the relationship with regard to tabes. Mott has shown (11) that tabes and general paralysis are expressions, with connecting links, of the late results of syphilis on the central nervous system. Fournier (12), as the result of his vast experience, positively affirmed that tabes and general paralysis were so alike in their etiology that they might be included under a common term, "parasymphilis." Krafft-Ebing (13) stated that general paralysis was the result of "civilisation and syphilisation," and after inoculating nine individuals suffering from general paralysis, who showed no signs of syphilis, with the virus of a hard chancre, waiting for 80 days, and finding then that none of them showed any symptoms, came to the conclusion that they were immune because they already had the disease. Finally, the fact that general paralytics give a positive Wassermann reaction in practically 100 per cent. of cases (14, 15, 16, 17) conclusively proves that if a positive Wassermann means syphilis, and it is a fact that the reaction is constant in the cerebro-spinal fluid or serum of general paralytics, then it amounts almost to a

demonstration that "no syphilis means no general paralysis." The only other view with any pretence to scientific support as to etiology is that of Ford-Robertson (18), who maintains that the organism isolated by himself and MacRae from the cerebro-spinal fluid of general paralytics, and named by them the "bacillus paralyticans," is the causal factor of the disease. O'Brien (19) has published a paper in support of the view, but other competent investigators, Marie (20), Chandler (21), Thomson (22), and Williamson (23), have either not been able to find the organism, or have found it as often in controls as in general paralytics, or have found that it exists as a common organism in the throat and skin in normal individuals, and cannot be considered the causal factor of the disease, or more than a secondary infection in general paralytics. Most alienists have therefore come to the conclusion that syphilis is a necessary precursor of the disease. [Anyone interested will find the views for and against syphilis discussed at length in Nonne.<sup>1</sup>] That syphilis is not the exciting cause seems, however, evident, since only from 3 to 5 per cent. of syphilitics develop tabes or general paralysis (Mott). In adults it is generally stated that alcoholic and sexual excess is responsible for tipping the scale, but in children excess "in baccho et venere" can generally be excluded, and so the stress of puberty is usually considered the exciting cause, the ordinary age of onset being from 13 to 15 years, though cases as early as 8 years of age, and as late as 23 years are recorded. The fact, however, that as a rule the reproductive organs are of the infantile type seems to weaken the assumption. One of McDowall's cases<sup>2</sup> was, notwithstanding, sexually well developed. Mott (24) mentions one case where a fall from a van seems to have been the exciting cause, and Collin (25) one of a boy who developed symptoms after an injured finger had been removed.

As to sex, in contradistinction to the adult type where 80 per cent. of the cases are male, in the juvenile type the sexes are almost equally divided, with perhaps a slight preponderance amongst females.

<sup>1</sup> Syphilis und Nervensystem. Berlin: S. Krager, 1909.

<sup>2</sup> Journal of Mental Science, January, 1908, p. 112.

Two mental and two physical types are found amongst these children. Mentally they may be defective from birth, ranging from idiots to high-grade imbeciles, or they may be bright and highly intelligent until the commencement of their illness. Physically they may show all the stigmata of congenital syphilis, or, as has been pointed out by Mott (26), may have absolutely no signs of syphilis whatever, whereas brother and sisters, not suffering from general paralysis, often have well-marked signs, as though the disease had spent itself on the cutaneous and bone lesions, and allowed the central nervous system to escape. It would seem, then, that it is more often in the mild or cryptic forms, those least likely to have had an adequate course of treatment, that the disease is more likely to show itself, and it is probable if it were not for the number of abortions, miscarriages, stillbirths, and deaths in early infancy, directly attributable to syphilis, the number of cases of juvenile general paralysis would be very much greater than has been found to be the case.

Assuming, then, that any congenital syphilitic may be a potential juvenile general paralytic, it becomes a vastly important matter, as pointed out by McDowall (27), to determine at what age we can safely assume that the children of known syphilitic parents are free from the risk of developing general paralysis. The average age of onset from Mott's statistics works out at 17, but he has had two cases occurring at the age of 23, and another at the same age is recorded by Burzio (28). Judging from statistics, then, the risk of a congenital syphilitic developing general paralysis after 25 years of age is very small, unless, indeed, as Mott suggests, it is possible for the adult type to occur as the result of the congenital as well as the acquired variety (29).

Turning now to individual details, it will perhaps be more interesting to describe the symptoms in the case recently under my care, comparing and contrasting them at the same time with those of the recorded cases and with the adult type.

The patient was a boy who was admitted to the East Sussex County Asylum as an imbecile. He was a good-looking, bright-eyed lad of apparently 8 years of age, though he was in reality 12, could answer simple questions, write his name rather badly,

but could not read or recognise colours. He was sent to the school for defective children attached to the asylum, proved rather dull, but was cheerful and well-behaved, and appeared to be in good health. In this state he remained for three years. In the interval his mother was admitted to the asylum as a general paralytic, an exceedingly uncommon coincidence, for though it is not rare for father and son each to develop general paralysis, it is extremely rare to find mother and son suffering from this disease in the same institution at the same time. This was the first intimation that the boy had a syphilitic heredity, as no details of his family history had been elicited when he was admitted, and he was free from all signs of syphilis, except two rounded smooth scars, one on either buttock, which were probably not syphilitic, as condylomata, which are quite common in that region in congenital syphilis, do not leave scars unless as the result of syphilo-sepsis?<sup>3</sup> After his mother's admission, however, he was kept under observation, but nothing developed until he was 16 years of age. He was then a bright, smiling high-grade imbecile looking about 10 years of age, able to run about and make himself useful, with a very limited but distinct vocabulary, and no apparent delusions.

On Sept. 21st, 1910, the boy suddenly developed a temperature of 102° F., and had retention of urine. Nothing was found in the chest or abdomen to account for the temperature, which subsided to normal in four days, during which time the patient had to be catheterised daily, a 24-hour specimen, amounting to 18 ounces, giving a specific gravity of 1032, containing 2·8 per cent. urea, no albumin, but a partial reduction of Fehling on testing for sugar. He lay smiling in bed, turned on his right side, with his knees drawn up, passively resisting attempts to straighten them. His bodily condition was fair, but the arms and legs were thin, and the genitals of the infantile type so commonly associated with the disease. The bowels only acted after enemata. The pupils were unequal, small, eccentric, oval, and sluggish to light. Accommodation could not be satisfactorily tested. There was no nystagmus, a rare condition

<sup>3</sup> The absence of signs of syphilis is not uncommon. Of Mott's 22 cases, 13 showed signs of syphilis, 9 did not. (Archives of Neurology, vol. i.).

which occurred only once in Mott's cases,<sup>4</sup> and no external ophthalmoplegia, a condition not uncommon in cerebral syphilis, but occurring again only once in Mott's cases (paralysis of the external rectus in Case 6). Both knee-jerks were exaggerated, as is usual in the disease, though in later stages it is not uncommon to find them absent on one or both sides. He never spoke, and had to be spoon-fed.

On Sept. 25th the patient was reported to have had a "seizure" in the night. During the following day he had eight typical epileptiform attacks. There was no cry, but he lay in bed with flushed, twitching face, his forehead and cheeks covered with large beads of perspiration. There was conjugate deviation of head, neck, and eyes to the right. The pupils were dilated and fixed. His right arm and leg twitched in unison with his grimacing face. When no attack was on there was a constant coarse tremor of the lips, and a curious, apparently unconscious, smacking as if after pleasant food. The tongue was protruded in a jerky manner, curled up at the tip, but was not markedly tremulous. Attacks occurred with diminishing frequency during the following week, and then ceased. Afterwards a crop of herpetic vesicles appeared on the lower lip. During the attacks loss of control of the bladder or rectum did not occur. Distinct paresis of the right face, the right arm, and the right leg followed the attacks, the superficial reflexes were very active, but there was no Babinski. Ankle-clonus was easily elicited on both sides (a rather uncommon occurrence), the knee-jerks were markedly exaggerated, wrist and triceps jerk well marked, but there was no jaw-jerk. Once or twice he vomited during an attack, a common occurrence in the "seizures" of general paralysis. There was no headache, judging from subjective signs. Under the action of homatropine the pupils dilated irregularly, showing pericyclic outlines. Examination showed optic atrophy, most marked in the right disc, but no chorio-retinitis. Watson (30) in 12 post-mortem examinations in such cases found optic atrophy in four, but this appears to be a much greater proportion than is found clinically. Chorio-retinitis, on the other hand, is not uncommon.

<sup>4</sup> Archives of Neurology, vol. i, p. 278.

Examination of the patient's serum showed a well-marked Wassermann reaction, 0·25 cubic centimetre of complement being fixed, whereas 0·1 cubic centimetre is usually required for diagnostic purposes. According to Nonne (31), a general paralytic should give the following reactions: (1) lymphocytosis in the cerebro-spinal fluid; (2) the globulin reaction; (3) Wassermann in the "fluid"; and (4) Wassermann in the serum. In a previous paper (32) he states, however, that the cerebro-spinal fluid may give a negative Wassermann in juvenile general paralysis, just as it does in 30 per cent. of the adult type.

On Oct. 2nd the facial palsy was seen to be improving, the brows corrugated naturally, the eyelids closed, but the lower half of the face remained as before. During the next fortnight the paresis of the right arm and leg improved till the grip was equal on both sides. The reflexes, however, were as active as during the "attacks," and both upper and lower limbs were so paretic that he could not sit up in bed, or attempt to feed himself. He was able, however, to shake hands, smile frequently, and to speak a few words very indistinctly. Urination was normal again.

The patient showed no symptoms of any delusions, as was to be expected in an imbecile. Indeed, the usual grandiose delusions of wealth, ambition, sexual power, or the inverted grandiose depression so equally characteristic of the adult type, are not to be expected in the juvenile form, even when attacking a previously normal intellectual child, because, as pointed out by Mott (8), "until puberty these passions have not formed a part of the experience of associative memory, have not been deeply organised in the brain, and so when the brain begins to decay, and the mind is shed, there are none of these passions present to rise uncontrolled into consciousness in pathological magnitude." This has been the general experience of most observers (33), but nevertheless there have been exceptions. One of Mott's cases thought he was a Member of Parliament, which, in the pauper class, may be considered an "idea of grandeur," and Kleineberger (34) records five cases with "childish ideas of grandeur."

During the month of October the patient's condition remained unchanged, except that at times he lost control of his

bladder and rectum, evacuating unconsciously ; and so, in spite of the fact that optic atrophy was present, it was decided to try the effects of "606" on him. Accordingly, on Oct. 30th, 0.3 gramme in solution was injected into the buttocks. No pain apparently was present after the injection, but the patient did not sleep as usual that night nor all the next day, and he frequently wrinkled his brow and put his left hand to his head in a puzzled manner. Eventually after 36 hours' sleeplessness he was given one-sixth of a grain of morphia, hypodermically, with good effect. After that he was able to sleep naturally without drugs.

The peculiar erythematous rash known as the "Jarisch-Herxheimer reaction" was not present in this case, a little local redness present at the seat of injection passing off in a few days. The temperature rose to 100° F. on the day after the injection, and continued above normal for six days. On Nov. 8th the patient developed atony of the bladder, associated with marked constipation, and had to be catheterised for two days. Such symptoms cannot, however, be ascribed to the drug, as he had had similar attacks twice before in the previous month.

Re-examined on Nov. 26th, four weeks after the injection, the patient's condition was as follows. Speech was more easily elicited, but was quite imbecile in character. Articulation was like that of a cleft-palate case. The pupils were unequal, the left reacting feebly to light under strong electric illumination, the right inactive. Reaction to accommodation could not be satisfactorily ascertained. The superficial reflexes were still exaggerated. Elbow-jerk, wrist-jerk, knee-jerk, and ankle-clonus well-marked and easily elicited. The bodily condition showed continued wasting since the injection. There was no difference in the fundus. Loss of control of bladder and rectum was present, and the patient was unable to stand or sit up.

It will thus be seen that there was practically no improvement, and this is in keeping with the vast majority of clinical reports recorded in the adult type and in tabes. At the outset Ehrlich cautioned against the use of "606" in degenerative changes, and in a recent communication to Sachs stated that

there had been 12 deaths in advanced cerebral and spinal disease after its use (35). In cerebral syphilis, however, Neisser states that paralysis and pains disappear like magic, and advises that it may be tried in early tabes and general paralysis, questioning, however, if it is safe when optic atrophy is present. From experiments on animals it has been found that "606" is not injurious to the normal eye, but in the human subject it is stated that transitory blindness may occur. Speithoff and Michaelis had a tabetic who 50 hours after an injection of 0.6 gramme was seized with temporary blindness for several minutes, and another who, eight weeks after an injection of 0.45 gramme, developed sudden ptosis of one lid and blindness lasting ten minutes. Nothing was found ophthalmologically (36). Glück treated two cases of paresis and one of optic atrophy without result (37). Fordyce<sup>5</sup> treated nine tabetics with little result, and one case of cerebral syphilis with wonderful success. Dr. Ivy Mackenzie reports that of 16 general paralytics four were undoubtedly benefited (38). Michaelis in one of his general paralytics had a remission lasting two months. In 12 paralytics treated by Meyer there was no lasting result. The Wassermann reaction after treatment in these cases of Meyer was very interesting; four gave a negative reaction, four a diminution, and four were uninfluenced (39). In this connexion it is interesting to note the extreme difficulty of influencing the Wassermann reaction by treatment in congenital syphilis. In the London Lock Hospital for Women and Children we found that even after two years' in-patient treatment by inunction children still gave an active Wassermann reaction; and McDonagh states that congenital syphilis, irrespectively of treatment, tends to give a positive Wassermann reaction throughout life (40). This statement, though there are strong reasons for believing that it is in the main correct, is probably not absolutely without exception, as the term "congenital syphilis" is at present loosely used to include cases both of infection before birth, in which the child is born dead, or if alive comes into the world with well-marked signs of syphilis, and cases of infection from the placental

<sup>5</sup> Loc. cit., *supra*.

blood, occurring during the period of delivery, and manifesting themselves some three or four weeks after birth.

Reverting again to the main subject, it will be seen from the cases quoted above that in syphilitic and parasymphilitic affections of the nervous system hopes of success may be entertained in cerebral syphilis, and that amelioration of symptoms in some tabetics and remissions in some general paralytics may follow the use of the drug. To anyone, however, acquainted with the frequent remissions, and even sometimes complete cessation of ataxic and mental symptoms, for a time in tabetics and general paralytics without treatment, the evidence that such improvement is due, in the cases quoted above, to the use of "606" is not convincing, and the necessity of early and systematic treatment to prevent these late manifestations becomes increasingly urgent. In Wassermann's reaction we apparently have a means of discovering latent congenital syphilis in the children of known syphilitics, and these are the cases that seem particularly liable to develop juvenile general paralysis. Considering, then, the apparent hopelessness of checking the malady by even the latest form of treatment, and the known fact that mercury has been proved time and again to be equally useless, it is imperative that such children should be given the very best possible chance at the earliest possible opportunity; and the mere fact that treatment has a very dubious effect on the character of the Wassermann reaction, instead of suggesting to us the impossibility of curing congenital syphilis, should stimulate us, on the contrary, to continue treatment, possibly for years, instead of, as is so frequently the case, stopping treatment as soon as the early manifestations during the first year of life subside.

Ehlers of Copenhagen reports a death five days after the injection of 0.5 gramme of "606" in a general paralytic.<sup>6</sup> The patient was a man, aged 40 years, who had developed syphilis 11 years previously and had been insufficiently treated. In April, 1908, he had an apoplectiform seizure. In August of the same year he first began to show signs of general paralysis (dementia paralytica). In July, 1910, he had a second seizure.

<sup>6</sup> Ein Todesfall nach Ehrlich-Hata: "606," Münchener Medicinische Wochenschrift, Oct. 18th, p. 2183.

On August 25th he was injected in the interscapular region subcutaneously with a neutral suspension after the manner of Wechselmann. His symptoms were those of poisoning; there was tremor, shivering, sweating, and progressive loss of strength. His temperature rose to  $103.6^{\circ}$  F. ( $39.8^{\circ}$  C.). He died from paralysis of the heart. A post-mortem examination showed all the organs to be healthy except the heart, in which there was acute parenchymatous degeneration. Details of the microscopic examination of the nervous system have not yet been published.

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